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REVIEW ARTICLE

Clearing the Air: A Review of the Effects of Particulate Matter Air Pollution on Human Health

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Abstract The World Health Organization estimates that particulate matter (PM) air pollution contributes to approximately 800,000 premature deaths each year, ranking it the 13th leading cause of mortality worldwide. However, many studies show that the relationship is deeper and far more complicated than originally thought. PM is a portion of air pollution that is made up of extremely small particles and liquid droplets containing acids, organic chemicals, metals, and soil or dust particles. PM is categorized by size and continues to be the fraction of air pollution that is most reliably associated with human disease. PM is thought to contribute to cardiovascular and cerebrovascular disease by the mechanisms of systemic inflammation, direct and indirect coagulation activation, and direct translocation into systemic circulation. The data demonstrating PM's effect on the cardiovascular system are strong. Populations subjected to long-term exposure to PM have a significantly higher cardiovascular incident and mortality rate. Short-term acute exposures subtly increase the rate of cardiovascular events within days of a pollution spike. The data are not as strong for PM's effects on cerebrovascular disease, though some data and similar mechanisms suggest a lesser result with smaller amplitude. Respiratory diseases are also exacerbated by exposure to PM. PM causes respiratory morbidity and mortality by creating oxidative stress and inflammation that leads to pulmonary anatomic and physiologic remodeling. The literature shows PM causes worsening respiratory symptoms, more frequent medication use, decreased lung function, recurrent health care utilization, and increased mortality. PM exposure has been shown to have a small but significant adverse effect on cardiovascular, respiratory, and to a lesser extent, cerebrovascular disease. These consistent results are shown by multiple studies with varying populations, protocols, and regions. The data demonstrate a dose-dependent relationship between PM and human disease, and that removal from a PM-rich environment decreases the prevalence of these diseases. While further study is needed to elucidate the effects of composition, chemistry, and the PM effect on susceptible populations, the preponderance of data shows that PM exposure causes a small but significant increase in human morbidity and mortality. Most sources agree on certain "common sense" recommendations, although there are lonely limited data to support them. Indoor PM exposure can be reduced by the usage of air conditioning and particulate filters, decreasing indoor combustion for heating and cooking, and smoking cessation. Susceptible populations, such as the elderly or asthmatics, may benefit from limiting their outdoor activity during peak traffic periods or poor air quality days. These simple changes may benefit individual patients in both short-term symptomatic control and long-term cardiovascular and respiratory complications.

Keywords Particulate matter · Air pollution · Cardiovascular · Respiratory · Public policy

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Introduction

While some correlation between poor air quality and human disease has been recognized since antiquity, the health effects of air pollution entered the world's consciousness in the twentieth century. In 1930, sulfur dioxide from local

factory emissions mixed with a dense fog over the Meuse Valley in Belgium. Over 3 days, several thousand people were stricken with acute pulmonary symptoms, and 60 people died of respiratory causes [1]. In December 1952, a dense smog containing sulfur dioxide and smoke particulate descended upon London, resulting in more than 3,000 excess deaths over 3 weeks and as many as 12,000 through February 1953 [2]. The lethality of air pollution was immediately recognized but not well understood. To this day, because the effects of air pollution on illness occur at a population level, many clinicians fail to appreciate the relationship between air pollution and health.

The 1970 Clean Air Act (CAA) was the first major American regulatory effort aimed at both studying and setting limits on emissions and air pollution. The 1970 CAA defined the National Ambient Air Quality Standards (NAAQS [3]). These standards set limits on six primary pollutants found in air: carbon monoxide, lead, nitrogen dioxide, ozone, sulfur dioxide, and particulate matter (PM) [4].

PM is a complex mixture of extremely small particles and liquid droplets made up of acids, organic chemicals, metals, and soil or dust particles [5]. Sources of PM are both natural and anthropogenic. Manmade sources of PM include combustion in mechanical and industrial processes, vehicle emissions, and tobacco smoke. Natural sources include volcanoes, fires, dust storms, and aerosolized sea salt.

PM can be described by its "aerodynamic equivalent diameter" (AED). Particles of the same AED will tend to have the same settling velocity. Researchers traditionally subdivide particles into AED fractions based on how the particles are generated and where they deposit in human airways: <10, <2.5, and <0.1 μm (PM_{10}, $PM_{2.5}$, and $PM_{0.1}$, respectively). Particles with a diameter greater than 10 μm have a relatively small suspension half-life and are largely filtered out by the nose and upper airway. Researchers define a diameter between 2.5 and 10 μm ($PM_{2.5–10}$) as "coarse," less than 2.5 μm as "fine," and less than 0.1 μm as "ultrafine" particles. When interpreting PM research, it is important to appreciate that PM_{10} contains ultrafine ($PM_{0.1}$), fine ($PM_{0.1–2.5}$), and coarse ($PM_{2.5–10}$) fractions. In a mixed environmental sample, the total number and total surface area of these particles *increases* exponentially as the diameter of the particle decreases. However, the total particulate mass of a substance generally *decreases* exponentially with decreasing particle diameter. For example, in a sample of PM_{10}, the numerical majority of particles would be ultrafine, but these particles would make up a negligible portion of the sample's total particulate mass (Fig. 1).

Studies show an increase in morbidity and mortality related to PM exposure. While the increased daily risks from PM exposure are modest for any individual, the costs of the worldwide healthcare burden are staggering when applied to populations. The World Health Organization estimates that $PM_{2.5}$ concentration contributes to approximately 800,000 premature deaths per year, ranking it the 13th leading cause of mortality worldwide [6].

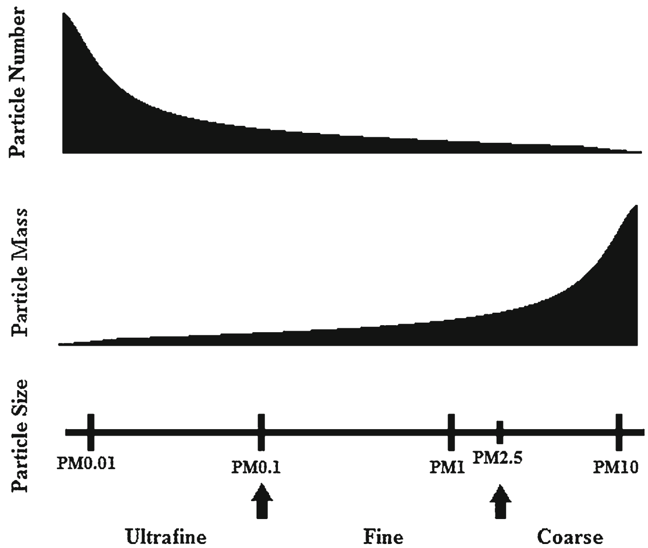

Fig. 1 A hypothetical mixed particle distribution

This paper provides a review of the effect of ambient airborne PM on human morbidity and mortality. We review the current understanding of the mechanisms that underlie the observed clinical findings. Emphasis is placed primarily on research concerning the cardiovascular, respiratory, and cerebrovascular systems. This review concludes with public health recommendations based on a summary of the reported literature's findings.

Methods

The authors conducted a scientific review of all available literature published over the last 30 years. Our primary objective was to determine the association or lack of association between PM and human health. Our secondary objective was to summarize the proposed mechanisms for any purported associations based on existing human, animal, and in vitro studies. We initiated a PubMed database search using the MESH terms "PM," "particulate matter," "air pollution," "ultrafine particles," "fine particles," "coarse particles," "PM10," "PM2.5," and "PM0.1." Articles were selected and agreed upon by the authors based on relevance and impact. Effort was made to provide both positive and negative studies where appropriate. Emphasis was placed on well-conducted trials and epidemiological investigations. Studies were only excluded for redundancy. After analysis of the available data, this paper concludes with individual and public health recommendations based on the existing scientific evidence.

PM and Cardiovascular Health Effects

Several large studies suggest that PM exerts significant effects on the cardiovascular system [7–9]. Research on this topic has focused on both the long-term effects of chronic PM exposure and the acute effects of increases in ambient PM on cardiovascular mortality. In a previous analysis [10], it was shown that for any increase in mortality caused by PM, two thirds of the effect was accounted for by the cardiovascular diseases.

Cardiovascular Mechanisms

Animal studies demonstrate a link between chronic PM exposure and the development of atherosclerosis via systemic inflammation [11, 12]. Human studies show that the effects appear to be mediated by the inflammatory cytokines IL-6, TNF-ά, and C-reactive protein (CRP). Increases in both IL-6 [13] and CRP [14] have been associated with the development of acute myocardial infarction. Ruckerl et al. [15] described transient IL-6 and TNF-ά elevations in diabetic patients for 2 days following PM10 exposure. In a prospective cohort study of German patients, Hoffman et al. [16] associated exposure to PM2.5 with elevations in CRP. Other researchers demonstrated similar increases in CRP from PM10 exposure from both combustion [17] and organic matter [18]. In contrast, some studies have found only a weak or absent link between PM and markers of inflammation [19–22]. Discrepancies among studies appear related to differences in composition of PM, variable exposure to anti-inflammatory medications, and differences in obtaining PM exposure data [10].

Acute exposure to PM causes changes in coagulation and platelet activation providing a more proximal link between PM and coronary artery disease. Many experts consider fibrinogen to be an important risk factor for cardiovascular disease [10]. Ruckerl et al. [15] associated a 5-day cumulative exposure to PM_{10} with increased fibrinogen levels in survivors of myocardial infarction. Other pro-coagulant factors, such as plasminogen activator fibrinogen inhibitor-1 (PAI-1), were also associated with PM elevations [17]. Intratracheal instillation of diesel exhaust particles led to increased platelet activation in hamsters and rapid thrombosis formation [23]. Further hamster studies also suggested that small particles translocate into the blood stream and exert prothrombotic effects [24]. Schicker et al. [18] showed that transient increases in PM10 exposure caused during hay-stacking increased platelet aggregation within 2 h of the activity. This activity also increased Von Willebrand factor and Factor VIII, markers of vascular endothelial activation.

Long-Term Effects

The “Harvard Six Cities study [7],” a cohort study published in 1993, followed 8,111 patients for 16–18 years and showed a 29% (95% CI, 8–47%) increase in the adjusted mortality rate for the most polluted of the cities compared to the least polluted. Particulate air pollution was positively associated with death from lung cancer and cardiopulmonary disease (Table 1).

Pope et al. [8] followed this in 1995 with another prospective cohort study of 552,000 patients in 151 metropolitan areas using the American Cancer Society's Cancer Prevention 2 database (ACS CPS 2). These data showed a 17% (95% CI, 9–26%) increase in all-cause mortality and a 31% (95% CI, 17–46%) increase in cardiopulmonary mortality when comparing the most and least polluted cities. In 2002 [25] and 2004 [26], Pope et al. re-reviewed the expanding ACS CPS 2 database, now with 1.2 million participants, and extended the follow up. Their research demonstrated an average increase in cardiopulmonary mortality of 9% (95% CI, 3–16%) for each 10-μg/m^3 increase in $PM_{2.5}$. Subsequently, they determined that a 10-μg/m^3 increase in PM increased ischemic cardiovascular disease mortality by 18% (95% CI, 14–23%) and mortality from arrhythmia, congestive heart failure, and cardiac arrest by 13% (95% CI, 5–21%).

In 2007, the Women's Health Initiative Study [27] followed a cohort of over 65,000 postmenopausal women with no previous

Table 1 Long-term effects of PM on the cardiovascular system

Author	Year	PM	ΔPM (in μg/m^3)	Outcome measure	Effect (95% CI)
Dockery et al. [17]	1993	PM_{10}	18.6	All-cause mortality	26% (8–47)
Pope et al. [18]	1995	PM_{10}	24.5	All-cause mortality	17% (9–26)
		PM_{10}	24.5	Cardiopulmonary mortality	31% (17–46)
Hoek et al. [28]	2002	BS	10.3	Cardiopulmonary mortality	71% (10–167)
Pope et al. [25]	2002	$PM_{2.5}$	10	Cardiopulmonary mortality	9% (3–16)
Pope et al. [26]	2004	$PM_{2.5}$	10	Ischemic CVD mortality	18% (14–23)
		$PM_{2.5}$	10	CHF, arrhythmia, CP arrest	13% (5–21)
Miller et al. [27]	2007	$PM_{2.5}$	10	Cardiovascular event	24% (9–41)
		$PM_{2.5}$	10	Cardiovascular mortality	76% (25–147)
Toren et al. [29]	2007	PM	Not measured	Cardiovascular mortality	12% (7–19)

PM particulate matter, *ΔPM* increase in ambient PM, *BS* black smoke

heart disease over approximately 6 years. The investigators revealed that long-term PM exposure in this population resulted in a 24% (95% CI, 9–41%) increase in cardiovascular events and an astonishing 76% (95% CI, 25–147%) increase in cardiovascular mortality per 10-μg/m^3 increase in $PM_{2.5}$. While these results had fairly wide confidence intervals, these data suggest that this cohort of patients may be particularly susceptible to ambient PM exposure.

The findings of cardiovascular effects from PM exposure are not unique to the USA. In the Netherlands, long-term exposure to traffic-related air pollution increased cardiopulmonary mortality by 71% (95% CI, 10–167%) [28]. A 2007 cohort study [29] of 250,000 Swedish construction workers from 1972 to 2002 found that workers with occupational PM exposure had a 12% (95% CI, 7–19%) increase in ischemic cardiovascular disease mortality.

While increases in PM have been consistently shown to increase cardiovascular morbidity and mortality, the effects of PM reduction have also been studied. In the 72 months following the ban of bituminous coal sales in Ireland in 1990, black smoke concentration decreased by 35.6 μg/m^3 over this time, and standardized respiratory and cardiovascular mortality decreased by 15.5% (95% CI, 12–19%) and 10.3% (95% CI, 8–13%), respectively [30]. An 8-year extension of the Harvard Six Cities data studied the population subset that moved from areas of higher to lower PM concentration [31], finding that a 10-μg/m^3 decrease in $PM_{2.5}$ resulted in a 27% (95% CI, 5–43%) decrease in overall mortality.

Short-Term Effects

A 2001 review [32] of 12 prior studies concluded that a 10-μg/m^3 increase in PM_{10} increased hospital admissions for congestive heart failure and ischemic heart disease by 0.8% (95% CI, 0.5–1.2%) and 0.7% (95% CI, 0.4–1.0%), respectively. Similarly, a 2006 review [33] showed a 0.44% (95% CI, 0.02–0.86%) and 1.28% (95% CI, 0.78–1.78%) increase in admissions for ischemic heart disease and heart failure for a 10-μg/m^3 increase in $PM_{2.5}$, respectively. In a smaller trial, Pope et al. [34] used a case-crossover of 12,000 patients in Utah to show that a 10-μg/m^3 increase in $PM_{2.5}$ led to a 4.5% (95% CI, 1.1–8.0%) increase in acute ischemic coronary events. In an analysis of PM concentrations from 20 major cities in the USA using the National Morbidity Mortality Air Pollution Study (NMMAPS) data, Samet et al. [9] showed a 10-μg/m^3 increase in PM_{10} caused an increase in all-cause and cardiopulmonary mortality by 0.5% (95% CI, 0.1–0.9%) and 0.7% (95% CI, 0.2–1.2%), respectively (Table 2).

Similar results have been found in Japan [35], Australia, and New Zealand [36]. In 2008, Samoli et al. [37] re-analyzed the data of the APHEA 2, NMMAPS, and several Canadian studies in order to assess the coherence of findings using the same methods for all three sets of data. They were able to show an increase in daily all-cause mortality for Canadian, European, and US cities. Interestingly, the short-term mortality resulting from acute increases in PM are not limited to the critically ill or dying. In fact, much of the mortality occurred among active individuals with one or more risk factors.

PM and Respiratory Health Effects

While much of the interest in PM has focused on the cardiovascular system [7, 8], many studies evaluated the association between PM exposure and respiratory illness. Researchers have evaluated endpoints including respiratory symptoms, medication use, lung function, health-care utilization, and mortality.

Table 2 Short-term effects of PM on the cardiovascular system

Author	Year	PM	ΔPM (in μg/m^3)	Outcome measure	Effect
Morris [32]	2001	PM_{10}	10	Hospital admission, IHD	0.7% (95% CI, 0.4–1.0)
		PM_{10}	10	Hospital admission, CHF	0.8% (95% CI, 0.5–1.2)
Domicini et al. [33]	2006	$PM_{2.5}$	10	Hospital admission, IHD	0.44% (95% CI, 0.02–0.86)
		$PM_{2.5}$	10	Hospital admission, CHF	1.28% (95% CI, 0.78–1.78)
Barnett et al. [36]	2006	$PM_{2.5}$	10	Hospital admission, IHD	1.6% (95% CI, 0.7–2.4)
		$PM_{2.5}$	10	Hospital admission, CHF	3.6% (95% CI, 1.8–5.4)
		$PM_{2.5}$	10	Hospital admission, AMI	2.7% (95% CI, 1.3–4.2)
Pope et al. [34]	2006	$PM_{2.5}$	10	Ischemic cardiac event	4.5% (95% CI, 1.1–8.0)
Samet et al. [9]	2000	PM_{10}	10	All-cause mortality	0.5% (95% CI, 0.1–0.9)
		PM_{10}	10	Cardiopulmonary mortality	0.7% (95% CI, 0.2–1.2)
Omori et al. [35]	2003	TSP	20	All-cause mortality	1.0% (95% CI, 0.8–1.3)
		TSP	20	Cardiopulmonary mortality	1.1% (95% CI, 0.7–1.5)

PM particulate matter, *ΔPM* increase in ambient PM, *TSP* total suspended particles, *IHD* ischemic heart disease, *CHF* congestive heart failure, *AMI* acute myocardial infarction

Respiratory Mechanisms

PM triggers pulmonary oxidative stress and inflammation. Human airway epithelial cells exposed to PM express inflammatory cytokines [38, 39]. Alveolar macrophages exhibit respiratory burst activity, producing reactive oxygen species, nitrogen species, and release TNF-ά and IL-1 after exposure [40]. In addition to oxidative stress generated from activation of inflammatory cells, reactive oxygen species may be directly generated from the surface of particles [41]. These responses can be potent and were shown to cause measurable pulmonary damage after only a single exposure in mice [42]. This oxidative damage is associated with the primary development of asthma and chronic obstructive pulmonary disease (COPD). Long-term exposure to PM results in airway remodeling and chronic inflammation [43]. PM may also contribute to asthma development by enhancing atopy and IgE responses [44, 45]. Several controlled human experiments have demonstrated adverse affects on the pulmonary system. PM exposure has been shown to increase airway responsiveness to methacholine [46], increase neutrophil numbers in bronchial lavage [47], decrease CO diffusion capacity, and decrease maximum mid-expiratory flow [48].

Respiratory Symptoms and Medication Usage

As part of the Children's Health Study, McConnell et al. [49] found that asthmatic children had a 40% (95% CI, 10–80%) increased risk of bronchitic symptoms for a 19-$\mu g/m^3$ increase in PM_{10}. Similarly, a 10-$\mu g/m^3$ increase in PM_{10} led to a 12% (95% CI, 4–22%) increase in severe asthma symptoms in Seattle children [50]. A study of inner-city asthmatic children revealed an association between $PM_{2.5}$ increases and missed school days for asthma [51]. A study of adult Parisians [52] showed a 41% (95% CI, 16–71%) increase in acute asthma exacerbations per 10-$\mu g/m^3$ increase in PM_{10}. Interestingly, nearly all PM levels in these studies were below levels set out in the NAAQS.

Respiratory medication use also increased in times of peak PM concentration. Use of rescue bronchodilators increased as ambient $PM_{2.5}$ rose in Denver [53] and the Northeast USA [54]. A review of 80,000 Alaskan Medicaid enrollees found prescription rates for bronchodilators increased by 18.1% and 28.8% when PM_{10} exceeded 34 and 61 $\mu g/m^3$, respectively [55]. Together, these data suggest that increases in ambient PM worsen asthma symptoms.

PM and Pulmonary Function

Several recent studies suggest that PM levels may affect lung function and lung development. The Children's Health Study [56] followed 1,759 patients over 8 years, finding that children who lived in communities with the highest PM concentrations were five times more likely to have low FEV1 than those in communities with the lowest PM concentrations. Moreover, children that moved from areas of higher to lower PM_{10} concentration had increased growth in lung function, and those that moved from areas of lower to higher PM_{10} concentration had decreased growth in lung function [57]. Even children with better lung function were susceptible to new onset asthma when exposed to higher levels of $PM_{2.5}$ [58]. Lower lung function has also been shown for children with cystic fibrosis exposed to higher levels of PM_{10} and $PM_{2.5}$ [59].

Similar inverse correlations between PM exposure and individual PEFR and FEV1 measurements have been reproduced internationally [60]. In the developing world, where indoor biomass burning can lead to PM levels exceeding 200 $\mu g/m^3$, researchers demonstrated that chronic exposure in children can lead to adult COPD, increased rates of lung infection, and impaired lung function [61].

In adults, effects of PM on lung function have been found primarily in susceptible populations. Investigators showed that asthmatic Londoners taking walks in areas of high PM had significantly higher reduction in FEV1, FVC, and increases in sputum biomarkers of inflammation [62]. In elderly patients, PM_{10} and $PM_{2.5}$ increases were associated with decreases in PEFR [63]. In COPD patients, decrements in lung function were associated with increases in $PM_{2.5}$ concentration [64]. Downs et al. [65] demonstrated that declines in PM_{10} concentration may actually lead to an attenuated decline in lung function in adult patients. However, research on healthy adults has not as consistently shown an association between PM and respiratory compromise [66].

PM and Respiratory-Related Healthcare Utilization

In a large case–control study [67], 10 $\mu g/m^3$ increases in $PM_{2.5}$ were associated with a 9% (95% CI, 4–14%) increase in bronchiolitis hospitalizations for infants. Large pediatric studies demonstrate increased asthma ED visits for increases in PM [68] and that PM_{10} increases of 6.5 $\mu g/m^3$ are associated with a 15% (95% CI, 2–30%) increase in respiratory-related hospital admissions [69] (Table 3).

For adults, several large studies have demonstrated an association between respiratory hospitalization and ambient PM_{10} [70] and $PM_{2.5}$ [71] concentrations. This includes admissions for asthma, COPD, and pneumonia. The effects appear to be stronger for elderly patients with even short-term exposures [72]. A study [73] of 12 million Medicare enrollees in 108 counties demonstrated significant increases in respiratory hospitalizations for increases in $PM_{2.5}$ in the Eastern USA. Because the same effects were not consistently observed in the Western USA, the authors suggested that morbidity may be related to the specific chemical constituents of PM which differs across the country. Several recent

Table 3 The effects of PM on respiratory admissions

Author	Year	PM	ΔPM (in μg/m^3)	Outcome measure	Effect (95% CI)
Karr et al. [67]	2006	$PM_{2.5}$	10	Infant bronchiolitis admissions	9% (4–14)
Lin et al. [68]	2005	$PM_{10–2.5}$	6.5	Pediatric respiratory admissions	17% (6–29)
Samoli et al. [92]	2011	PM_{10}	10	Pediatric asthma admissions	2.54% (0.06–5.08)
Peng et al. [93]	2008	$PM_{10–2.5}$	10	Respiratory admissions	0.33% (−0.21–0.86)
Zanobetti et al. [70]	2009	$PM_{2.5}$	10	Respiratory admissions	2.07% (1.2–2.95)
		$PM_{2.5}$	17	Pneumonia admissions	6.5% (1.1–11.4)
Medina-Ramon et al. [71]	2006	PM_{10}	10	COPD admissions	1.47% (0.93–2.01)
		PM_{10}	10	Pneumonia admissions	0.84% (0.5–1.19)
Dominici et al. [33]	2006	$PM_{2.5}$	10	COPD admissions	1.61% (0.56–2.66)
McGowan et al. [77]	2001	PM_{10}	14.8	Respiratory admissions	3.37% (2.34–4.40)
Ostro et al. [94]	2009	$PM_{2.5}$	14.6	Pediatric respiratory admissions	4.1% (1.8–6.4)

PM particulate matter, *ΔPM* increase in ambient PM

large studies have provided further evidence that the strength of PM effect may depend on the composition [74]. Investigations in European cities [75], Asian cities [76], and Oceania cities [77] have demonstrated a consistent and small though significant association between PM concentrations and emergency visits for respiratory diseases.

PM and Respiratory Mortality

The Six Cities study [7], 20 cities study [9], and ACS CPS 2 [8] cohort revealed an association between PM exposure and cardiopulmonary mortality. These studies did not, however, separate the impact on respiratory mortality versus cardiovascular mortality. A follow-up investigation using data from the 20 Cities Study revealed a 0.87% (95% CI, 0.38–1.36%) increased respiratory mortality for short-term increases in PM_{10} by 10 μg/m^3 [78]. This was subsequently expanded into a larger cohort of 112 US cities, where researchers found a 1.68% (95% CI, 1.04–2.33%) increase in respiratory mortality for every 10-μg/m^3 increase in $PM_{2.5}$ [79]. A study of California counties similarly revealed an increased respiratory mortality with increases in PM_{10} [80].

These results have been reproduced in countries around the world. A Norwegian study [81] demonstrated a 17% (95% CI, 9–25%) increase in mortality risk from COPD for every quartile increase in $PM_{2.5}$. In a study of 275,000 adults in ten Italian cities [82], short-term PM_{10} increases led to a 2.29% (95% CI, 1.03–3.58%) increase in respiratory mortality. Similar results for increased respiratory mortality have been found in Asian cities where researchers have demonstrated excess respiratory mortality risk for increases in PM_{10} [83]. Nearly identical effect sizes for respiratory mortality were found in the APHEA2 trial which studied this relationship across 29 European cities [84]. One study even demonstrated an association between PM_{10} and respiratory mortality in children under age five [85] (Table 4).

PM and Cerebrovascular Health Effects

Ischemic cerebrovascular and cardiovascular disease share many risk factors, features, and pathophysiological mechanisms. As an example, CRP, similar to cardiovascular disease, has also been implicated in the genesis of stroke [86].

Table 4 The effects of PM on respiratory mortality

Author	Year	PM	ΔPM (in μg/m^3)	Outcome measure	Effect (95% CI)
Zeka et al. [78]	2005	PM_{10}	10	Respiratory mortality	0.87% (0.38–1.36)
Zanobetti et al. [79]	2009	$PM_{2.5}$	10	Respiratory mortality	1.68% (1.04–2.33)
Wong et al. [83]	2008	PM_{10}	10	Respiratory mortality	0.62% (0.22–1.02)
Analitis et al. [84]	2006	PM_{10}	10	Respiratory mortality	0.58% (0.21–0.95)
Hales et al. [91]	2010	PM_{10}	10	Respiratory mortality	1.3% (0.5–2.1)
Pope et al. [25]	2002	$PM_{2.5}$	10	Lung cancer mortality	8% (1–16)
Ostro et al. [80]	2006	$PM_{2.5}$	10	Respiratory mortality	2.2% (0.6–3.9)

PM particulate matter, *ΔPM* increase in ambient PM

However, the evidence linking PM and stroke is more sporadic and the mechanisms less well understood.

Dominici et al. [33] reviewed an air quality data for 204 US urban counties and showed that a 10-μg/m^3 increase in ambient $PM_{2.5}$ increased the risk of hospitalization for cerebrovascular events by 0.8% (95% CI, 0.3–1.3%). A separate review [87] of Medicare patients found an increase of 1.03% (95% CI, 0.04–2.04%) for hospital admission for ischemic stroke for each 10-μg/m^3 increase in PM_{10}. Still other investigators found a previous day $PM_{2.5}$ increase of 5.2 μg/m^3 led to a 3% (95% CI, 0–7%) increase in risk of TIA and ischemic stroke.

In contrast, a recent large prospective multi-center stroke registry found no increase in the general population for ischemic stroke from exposure to $PM_{2.5}$. There was, however, an 11% (95% CI, 1–22%) increase in stroke risk in exposed patients with diabetes [88]. A large case-crossover study found an association between other components of air pollution (NO2 and CO) and cerebrovascular disease, but no correlation was noted with changing PM levels [89]. Similarly, a large registry of first-ever strokes found no association with PM_{10} for ischemic or hemorrhagic stroke [90].

There are several reasons why studies of PM and cerebrovascular disease have produced conflicting results. Some studies do not completely adjust for all confounding variables. There is further heterogeneity due to differences in the definition of cerebrovascular disease, or whether pollution is measured on the day of admission or symptom onset [88]. Further, it is possible that exposure to PM may not contribute to an overall increase in cerebrovascular disease, but only trigger events in vulnerable populations.

Recommendations and Conclusions

In evaluating the literature, there appears to be a small, but consistent and significant, effect of PM on human health. Overall, the small individual effects result in a large global public health burden. Notably, the effects are most pronounced for cardiovascular disease. Several studies have demonstrated an increase in cardiovascular mortality and hospitalizations. There are similar effects, of smaller amplitude, in respiratory disease. More study is needed to clarify the relationship between PM and cerebrovascular disease.

There are limitations to much of the available PM research. Most studies do not use individual exposure data. Rather, air monitors in population centers are used as surrogates for individual exposure. Even after adjusting these data for time spent in traffic, exposure to second-hand smoke, etc., estimates may not be accurate. Despite these limitations, different types of studies conducted in different locations find similar results. A dose–response relationship between PM exposure and adverse effects has been identified, and improvement in health endpoints is observed when the PM exposures are reduced. Overall, the available evidence suggests a causal association between long- and short-term PM exposure and cardiovascular and respiratory morbidity and mortality.

Further research is still needed to fully understand how PM affects human health. While studies show increased PM concentration has adverse health affects, the actual composition of particulates that is harmful has not yet been elucidated. Further studies are also needed to clarify the time course of PM-induced effects. In limited studies, some effects seem to appear within hours, while other reach their zenith within several days peak PM exposure. The data on this "lag time" effect can

Table 5 Air quality index and recommendations

AQI level	AQI value	$PM_{2.5}$	PM_{10}	Actions to protect your health from particle pollution
Good	0–50	0–15	0–50	None
Moderate	51–100	16–35	51–154	Unusually sensitive people should consider reducing prolonged or heavy exertion
Unhealthy for sensitive groups	101–150	36–65	155–254	Susceptible groups[a] should reduce prolonged or heavy exertion Everyone else should limit prolonged or heavy exertion
Unhealthy for sensitive groups	151–200	66–150	255–354	Susceptible groups[a] should avoid all physical activity outdoors Everyone else should avoid prolonged or heavy exertion
Very unhealthy	201–300	>150	>354	Susceptible groups[a] should remain indoors and keep activity levels low Everyone else should avoid all physical activity outdoors

EPA-456/F-09-002

Air quality index: a guide to air quality and your health. EPA, August 2009

AQI air quality index

[a]People with heart or lung disease, children, or older adults

be contradictory, and this phenomenon remains incompletely understood. The true biological mechanisms leading to PM-induced pathology continue to be investigated. Also, while regional exposure data has become standard for PM epidemiology, studies with true individual exposure have yet to be fully realized. Finally, studies defining susceptible populations will help to shape further population-based recommendations.

Clinical Recommendations

When a patient presents with an acute illness, the clinician will not be able to determine the degree to which PM contributed. In illnesses where PM is known to contribute to risk, that percentage risk increase is usually measured in the single digits. Therefore, it is unlikely that there will ever be specific therapies for PM-related illness. Rather, health care providers should be familiar with prevention strategies for PM-related illness. Indoor PM exposure can be minimized by using air conditioning, particulate air filters, avoiding use of indoor combustion for cooking and heating, and smoking cessation [95]. Susceptible groups may benefit from limiting their outdoor exercise during peak traffic periods or poor air quality days [96]. The Air Quality Index (AQI) (http://airnow.gov) provides up-to-date information regarding local concentrations of PM and other pollutants. While government agencies have put out recommendations for minimizing PM exposure, peer-reviewed controlled data are limited for the implementation of these recommendations (Table 5).

Though PM exposure is ubiquitous, there is no defined and studied “safe” level. Patient education and behavioral modification strategies may contribute to better overall health. Additionally, these data can enable policy makers, after weighing the economic impact, to enforce or strengthen existing legislation that limits PM exposure. Volcanoes, forest fires, and other natural PM sources are part of our world and are unavoidable. However, by reducing modifiable PM exposure, we will likely see reductions in morbidity and mortality.

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